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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,108	09/25/2003	Homme W. Hellinga	180/106	8184

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,108	HELLINGA ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-56* is/are pending in the application.

4a) Of the above claim(s) *42-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II in the reply filed on June 24, 2005 is acknowledged. The traversal is on the ground(s) that it is not unduly burdensome to search the sequences identified as SEQ ID NO:5-23, since they are similar. This is not found persuasive because applicants' traversal is not on the grounds that the sequences are not patentably distinct, rather that these distinct sequences are similar.

Applicants' argue that there would be no serious burden on the Examiner to search for the other sequences. However, in the instant case these sequences are unrelated and distinct and the search of the polypeptides and the polynucleotides are not coextensive. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to a particular polypeptides which would not have described other polypeptides or polynucleotides. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. This search requires an extensive analysis of the art retrieved in a sequence search and will require an in-depth analysis of technical literature. The scope of polynucleotides as claimed extends beyond the polynucleotide that encodes the claimed polypeptides as explained above. As such, it would be burdensome to search all the sequences together. It is also noted that applicant has not submitted evidence or

clearly admitted on the record that the sequences are obvious variants, which further implies that an unduly burdensome search is required to search each separate and distinct sequence. Therefore the requirement is still deemed proper and is made FINAL.

Amendment Entry

2. The amendment of September 25, 2003 has been entered. The examiner acknowledges the amendments to the specification. Claims 1-31 have been cancelled. Claims 42-56 have been withdrawn from consideration. Claims 32-41are drawn only to SEQ ID NO:5 and 6 are under consideration in this office action.

Priority

3. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C.120, a specific reference to the prior-filed application which is now US Patent number 6,663,862 in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 32 and 35-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to an isolated nucleic acid molecule encoding the B1 domain of Streptococcal protein G (GB1) domain polypeptide which binds a Fab fragment of an Immunoglobulin G (IgG) but does not bind an Fc fragment of IgG.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc.,107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas,

etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Furthermore, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the

disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. In this case, the nucleic acid molecule encodes the B1 domain of Streptococcal protein G (GB1) domain polypeptide which binds a Fab fragment of an Immunoglobulin G (IgG) but does not bind a Fc fragment of IgG, however no structure for this nucleic acid has been claimed. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In *Gostelli*, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

The written description in this case sets forth specific sequences, however an isolated nucleic acid molecule encoding the B1 domain of Streptococcal protein G (GB1) domain polypeptide which binds a Fab fragment of an Immunoglobulin G (IgG) but does not bind a Fc fragment of IgG is not commensurate in scope. Thus applicants were not in possession of a nucleic acid molecule defined only by its function, i.e., the ability to encode the B1 domain of Streptococcal protein G (GB1) domain polypeptide and bind to a Fab fragment of an Immunoglobulin G (IgG) but not bind a Fc fragment of IgG. Thus any molecule, which encodes the GB1 domain, is encompassed by the claims, yet applicants were not in possession of all those nucleic acid molecules simply on the basis of their function. Thus, the resulting nucleic acid molecules could result in a molecule not taught and enabled by the specification.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is

unquestionable that claim 32 is a broad generic claim with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of polymer with any biomolecule. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient as a characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, the claims recite some functional characteristics, yet the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples of the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. The specification is limited to the above mentioned sequences. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

5. Claims 32-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Acronyms like "GB1" and "IgG" in claim 32 must be spelled out when used for the first time in a chain of claims.

6. Claims 35-38 are unclear. For instance, claim 36 is drawn to the molecule being further defined as positioned under the control of a promoter. How does the position of the promoter further define the molecule? Thus a molecule being further defined as positioned under the control of a promoter is unclear and appropriate clarification is required to overcome the rejection. Likewise, claims 35 and 37 further define the nucleic acid in terms of a DNA segment and a recombinant vector, therefore clarification is required to overcome the rejection of these claims also.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 32 and 35-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Fahnestock et al., (US Patent 4,977,247 published December 11, 1990).

The claims are drawn to an isolated nucleic acid molecule encoding the B1 domain of Streptococcal protein G (GB1) domain polypeptide which binds a Fab fragment of an Immunoglobulin G (IgG) but does not bind a Fc fragment of IgG. The dependant claims are drawn to DNA segments, recombinant expression vectors and host cells.

Fahnestock et al., teach the identification of nucleic and amino acid sequences for the active binding sites of Protein G molecules (col. 4, lines 52-55). The invention also provides for Protein G genes being inserted into cloning vectors via recombinant technology (col. 4, lines 63-68). Chromosomal DNA was isolated from Streptococcal strains (col. 5, lines 37-39). The DNA fragments were inserted into cloning vectors, whereby any suitable plasmid or bacteriophage vector may be used (col. 5, lines 50-53). The cloned Protein G may be inserted into a variety of expression vectors and comprise regulatory regions that include DNA sequences necessary for expression (col. 7, lines 29-35). In accordance with conventional methods, other expression signals may be contained in an expression vector, where the host cell is *E.coli* or a bacteriophage and either expression vector further comprises promoters/operators (col. 7, lines 45-49). Also the intended microbial host cells will aid in the identification of host cells that have been transformed by the vector (col. 5, lines 54-59). Variants can be encoded by genes whose coding sequence are from the B1 and/or B2 and hybrid B1 and B2 binding domains (col.9-16, lines 67-68). The variants may be used to isolate the Fab or F(ab')2 fragments from IgG. Moreover, chromatography conditions affect and determine the binding Fab and Fc fragments, see tables 2 and 4 (col. 52 and 53). Therefore,

Fahnestock et al., teach a nucleic acid molecule as claimed since the ability of the Fc fragment is determined by chromatography conditions.

Thus, Fahnestock et al., clearly teach an isolated nucleic acid molecule encoding the B1 domain of Streptococcal protein G (GB1) domain polypeptide which binds a Fab fragment of an Immunoglobulin G (IgG) but does not bind a Fc fragment of IgG which is comprised within a recombinant expression vector and a host cell.

8. Claims 32 and 35-40 are rejected under 35 U.S.C. 102(a) as being anticipated by Sloan et al., (Protein Engineering, 1998).

The claims are drawn to an isolated nucleic acid molecule encoding the B1 domain of Streptococcal protein G (GB1) domain polypeptide which binds a Fab fragment of an Immunoglobulin G (IgG) but does not bind a Fc fragment of IgG. The dependant claims are to DNA segments, recombinant expression vectors and host cells.

Sloan et al., teach the interaction between the residue B1 domain of Streptococcal protein G (GB1) and the constant domain fragment of human immunoglobulin IgG (hFc) by engineering single cysteine mutations in GB1 (page 819, para. 2). The gene from plasmid pGB1 was recloned into M12mp18 where mutations were introduced into the oligonucleotide single stranded DNA mutants genes which were recloned behind the *tac* promoter of the pKK223-2 expression vector purchased from Pharmacia (page 820, para.3). Therefore, Sloan et al., teach an isolated nucleic acid molecule with a DNA segment comprised within a recombinant expression vector

under the control of a promoter, just as required by the claims. *E.coli* cells were freshly transformed with the expression construct (page 820, para.4). Thus, Sloan et al, teach recombinant host cells. It was found that none of the conjugates at position 36 showed any change in fluorescence upon the addition of the Fc fragment (page 821, para.4). Table I shows the binding behavior of the construct at position 36 which did not bind to the Fc fragment (page 822).

Thus, Sloan et al., clearly teach an isolated nucleic acid molecule encoding the B1 domain of Streptococcal protein G (GB1) domain polypeptide which binds a Fab fragment of an Immunoglobulin G (IgG) but does not bind a Fc fragment of IgG which is comprised within a recombinant expression vector and a host cell.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claim 32-33 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 5-6 of U.S. Patent No.

6,663,862. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent and the instant claims are drawn to a B1 domain of protein G (GB1) polypeptide. The patent is drawn to an isolated GB1 polypeptide which maintains binding activity for a Fab fragment of IgG but exhibits substantially no binding activity for the Fc fragment. Furthermore, claim 6 of the patent is drawn to the polypeptide having the amino acid sequence of SEQ ID NO:6.

The instant claims are drawn to an isolated nucleic acid molecule encoding the B1 domain of Streptococcal protein G (GB1) domain polypeptide which binds a Fab fragment of an Immunoglobulin G (IgG) but does not bind a Fc fragment of IgG. Thus the same polypeptide is encoded. Furthermore, instant claim 33 is drawn to the encoded polypeptide comprising the amino acid sequence of SEQ ID NO:6. Therefore the claims of both the patent and the instant claims are drawn to an encoded the B1 domain of Streptococcal protein G (GB1) domain polypeptide which binds a Fab fragment of an Immunoglobulin G (IgG) but does not bind a Fc fragment of IgG. Furthermore, US Patent and the instant claim recite encoding the same sequence. Therefore, the instantly claimed encoded polypeptide is not patentably distinct from polypeptide of the patent.

Prior Art

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Eliasson et al., teach structural and functional analysis of the human IgG-Fab receptor activity of streptococcal protein G. Huth et al., teach designs of an expression system for detecting folded protein domains and mapping macromolecular interactions by NMR.

Conclusion

12. No claims allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines

September 5, 2005